

REMARKS/ARGUMENTS

Claims 1-28 are pending in the application. Claims 1-27 remain subject to a restriction requirement. Claims 1-9, 14-18, and 25-28 are directed to the subject matter elected without traverse. Claims 10-13 and 19-24 are directed to the non-elected subject matter and have been withdrawn from further consideration by the Examiner.

Claims 2-9, 14-18, and 25-27 are currently amended. New Claim 28 has been added to require the two sharp peaks at 2θ angles of 5.856 and 6.99° which are optional in original Claim 1. Claims 2-9 and 14 have been amended to replace the term “substance” with “monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1- bisphosphonic acid in an amorphous form” for express antecedent basis in Claim 1. Claim 14 has been amended to clarify the “formula I in the crystalline form” is the monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1- bisphosphonic acid as disclosed at page 1, lines 5-6, of the Specification. Claims 15-17 have been redrafted to replace the term “substance” with the term “form” for express antecedent basis in Claim 14. Claims 25 and 27 have been redrafted to replace “active substance” with a monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1- bisphosphonic acid in an amorphous form for express antecedent basis in Claim 1. All other changes to Claims 2-9, 14, 16-18, and 25-27 are editorial in nature. Claim 15, however, has been redrafted to remove the Examiner’s objection to the phrase “used in the form” therein and substitute language which limits the crystalline form of formula I to which Claim 15 refers to the pentahydrate, as Applicant originally intended. As a result, Applicant believes the Examiner’s objections to the language of Claim 15 and rejections of Claim 15 under 35 U.S.C. §101 and §112, first para., bridging pages 7 and 8, and objections to the terms “substance” and “active substance” in Claims 2-9, 14-18, and 25-27 for lack of antecedent basis in Claim 1 and rejections under 35 U.S.C. §112, 2nd para., in the Official Action (OA) mailed May 9, 2008, have been overcome and should be withdrawn.

Rejections under 35 U.S.C. § 112, 2nd para.

1. Antecedent basis for terms in Claims 2-9, 14-18, and 25-27

The Examiner concluded that Claims 2-9, 14-18, and 25-27 are indefinite because (OA, p. 7), “No antecedent basis can be found for the term substance in claims 2-9, 14-18, and 25-27. Further, the term is indefinite [as] to its meaning.” As per the current amendment, the term “substance” has been removed from all dependent claims and replaced by reference to the monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1- bisphosphonic acid in an amorphous form expressly recited in Claim 1. Accordingly, the Examiner’s rejections of Claims 2-9, 14-18, and 25-27 under 35 U.S.C. § 112, 2nd para., for lack of antecedent basis should be withdrawn.

2. Meaning of the phrase “in an amorphous form” in Claim 1

Claims are to be interpreted primarily from the claim language itself, and when that language is unclear, based on the definitions thereof in the supporting specification. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-1315 (Fed. Cir. 2005)(en banc). Claims, read in light of the specification, need only reasonably apprise persons having ordinary skill in the art of their scope and be as precise as the subject matter permits. *Hyrtech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385 (Fed. Cir. 1986).

The focus of the Examiner’s objection to, and rejection of, Applicant’s Claim 1 and all claims dependent thereon under 35 U.S.C. §112, 2nd para., stems from what the Examiner perceives as an indefinite recitation of a “salt . . . in an amorphous form, having the X-ray diffraction pattern showing characteristic broad obtuse peak at 2θ angles ranging from 15 to 25 °, and, optionally, two sharp peaks at 2θ angles of 5.856 and 6.99° ” in Claim 1. According to the Examiner, the X-ray diffraction pattern of an amorphous form of a salt cannot show two sharp peaks (OA, p. 7). According to the Examiner (OA, p. 7):

Any X-ray diffraction of an amorphous material is only to show no diffraction or non-crystalline, *i.e.*, a single broad, shallow peak termed an *amorphous halo*. Note pages 578-579 of Nerurkar et al.

The Examiner's appears to criticize Applicant's claim language because it allows the X-ray diffraction pattern of the claimed monosodium risedronate salt in an amorphous form to exhibit a sharp peak other than the "single broad shallow, peak" referred to in the art as an "amorphous halo" (OA, p. 7). According to the Examiner, an X-ray diffraction pattern with no diffraction peaks conventionally shows that a substance is present in the amorphous form. On the other hand, the Examiner finds that an X-ray diffraction pattern with peaks conventionally shows that the substance is present in the crystalline form (OA, p. 7).

The Examiner's criticism, however, is based entirely on a conventional, more general definition of a salt described "in an amorphous form", not the more specific definition Applicant employs to define a monosodium salt of risedronic acid in an amorphous form in the present Specification. Therefore, Applicant respectfully suggests that the Examiner misinterpreted and misunderstood the full scope and content of the subject matter Applicant claims.

A patent applicant is generally free to be his own lexicographer and define terms in a claim contrary to their ordinary meaning. Terms in a claim will be given their ordinary and customary meaning unless it is apparent from the specification that the inventor used the terms differently. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357 (Fed. Cir. 1999); *ZMI Corp. v. Cardiac Resuscitator Corp.*, 844 F.2d 1576, 1580 (Fed. Cir. 1988).

In this case, the Examiner should not have focused on the general, customary meaning of the phrase "in an amorphous form" when interpreting the scope and content of Applicant's claims and the conventional XRD patterns of amorphous forms of other known substances because it would have been apparent to a person having ordinary skill in the art that

Applicant's Specification defines the phrase "in an amorphous form" to encompass new and different kinds of amorphous forms.

On consideration of Applicant's disclosure, persons having ordinary skill in the art would have learned that Applicant's invention is directed to "new amorphous forms" (Spec., p. 3, ll. 19-20). The "new amorphous forms" include: (1) amorphous forms having unique X-ray diffraction patterns where sharp peaks characteristic of a crystalline phase of the form are not observed (Spec., p. 3, ll. 27-28), and (2) "virtually amorphous" or "semi-crystalline forms" having X-ray diffraction patterns which are uncharacteristic of pure crystalline forms, uncharacteristic of pure amorphous forms, and uncharacteristic of mixtures of crystalline and amorphous forms of monosodium risedronic acid (Spec., p. 4, ll. 6-15), i.e., X-ray diffraction patterns characterized by two sharp peaks at 2θ angles of 5.85 and 6.99° (Spec., p. 4, ll. 17-26). The "new amorphous forms" Applicant claims may contain up to 10 % water, are stable under normal conditions, and appear to be suitable for pharmaceutical formulations (Spec., p. 4, l. 30, to p. 5, l. 2, and p. 5, l. 19, to p. 6, l. 2).

The Examiner is correct that Applicant's claims are directed to "amorphous form[s]" which display the X-ray diffraction patterns in-part conventionally exhibited by amorphous forms of other types of compounds and in-part unconventionally exhibited by amorphous forms of the other types of compounds. Nevertheless, free to be his own lexicographer in his Specification, Applicant defines "in an amorphous form" in an unconventional manner. The examiner should give terms in applicant's claim their ordinary and customary meaning unless, as is here the case, the supporting specification teaches that the inventor defined and used the terms differently. Here, Applicant's Specification defines the term "in an amorphous form" as including virtually amorphous or semi-crystalline forms. Consistent therewith, the claimed monosodium salt of risedronic acid "in an amorphous form" is

characterized by X-ray diffraction patterns which may, and optionally, may not be unconventional.

In light of the teaching in Applicant's Specification, it is unreasonable for the Examiner to maintain the rejection of Applicant's claims under 35 U.S.C. § 112, 2nd para.. Applicant's claims are as precise as the subject matter permits, and when read in light of the supporting Specification, would have reasonably apprised persons having ordinary skill in the art of their scope. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385 (Fed. Cir. 1986). Properly, the Examiner's rejection of Claims 1-9, 14-18, and 25-27 under 35 U.S.C. § 112, 2nd para., because the claimed monosodium salt of risedronic acid "in an amorphous form" optionally shows an unconventional X-ray diffraction pattern, should be withdrawn. The claims are as precise as the subject matter permits and reasonably apprise persons having ordinary skill in the art of their scope.

Rejections under 35 U.S.C. § 103

The Examiner rejects Claims 1-9 and 25-27 under 35 U.S.C. § 103(a) as unpatentable in view of the combined teachings of Cazer (U.S. 6,410,520), Turchetta (US 2005/0215793), Brittain (Polymorphism in Pharmaceutical Solids, pp. 1-2 and 183-226, 1999), Threifall (Analyst, vol. 120, pp. 2435-60, 1995), and Muzaffar (J. Pharm., vol. 1(1), pp. 59-66, 1979).

1. Turchetta

The Examiner has not established that Turchetta is prior art under 35 U.S.C §102(e) or any other basis. Turchetta is a U.S. Patent Publication filed February 28, 2005. On its face, Turchetta refers to Provisional Application No. 60/558,908, filed on April 1, 2004. Applicant's present application was filed as International Application PCT/CZ2005/000024 on February 28, 2005, and claims benefit of foreign priority under 35 U.S.C. §119 based on Czech Republic Applications PV 2004-292, filed February 26, 2004; PV 2004-798, filed July 8, 2004; and PV 2004-880, filed August 12, 2004. To apply Turchetta as prior art under 35

U.S.C. §102(e) to the subject matter Applicant presently claims, the Examiner has the preliminary burden to establish that Turchetta is entitled to benefit of the April 1, 2004, filing date of related provisional application 60/588,908. This the Examiner has not done. Moreover, we are lost trying to understand how the disclosure of Turchetta's provisional application which relating to a lyophilized amorphous form of sodium risedronate would have satisfied the requirements of 35 U.S.C. §112, 1st and 2nd paragraphs, when the Examiner alleges that Applicant's present disclosure does not satisfy the requirements of 35 U.S.C. §112, 1st and 2nd paragraphs, for any of the subject matter presently claimed. While not conceding that Turchetta is prior art to the subject matter Applicant presently claim, we hereafter reply to the Examiner's rejection under 35 U.S.C. §103 in view of art including Turchetta as if Turchetta was prior art under 35 U.S.C. §102(e) to advance prosecution. However, we continue to deny that the Examiner has established the prior art status of Turchetta's disclosure in this case.

The Examiner has not explained the significance of Turchetta's teaching to the rejection of Applicant's claims under 35 U.S.C. §103 for obviousness in view of the combined teachings of Cazer, Turchetta, Brittain, Threifall, and/or Muzaffar. Applicant suspects that the Examiner is relying on Turchetta for its description of sodium risedronate in an amorphous form. However, the sodium risedronate in an amorphous form described by Turchetta is characterized by (1) the X-ray diffraction spectrum of Turchetta's Figure 1 (Turchetta, p. 2, col. 2, Claim 1) and (2) the processes of making sodium risedronate in an amorphous form of Claims 2 to 12 (Turchetta, p. 2, col. 2, Claim 2), in addition to (3) the use sodium risedronate in an amorphous form so described for treating diseases relating to calcium metabolism (Turchetta, p. 2, col. 2, Claims 13-14). Unlike the X-ray diffraction patterns of the salt in an amorphous form defined by Applicant's claims, the salt in the

lyophilized amorphous form which Turchetta appears to have analyzed has an X-ray diffraction pattern which shows (Turchetta, Figure 1):

- (1) a broad obtuse peak at 2θ angles ranging from 11.5 to 23.5° with its apex at 17.0°,
- (2) a distinct peak at a 2θ angle of 9.3°,
- (3) a broad obtuse peak at 2θ angles ranging from 5 to 8.5° with its apex at 7.2°, and
- (4) a broad obtuse peak at 2θ angles ranging from 25.5 to 31.5° with an apexes at 29.0 and 30.8°.

The comparatively different X-ray diffraction pattern of the salt in the amorphous form defined by Turchetta's Claim 1 and the salt in an amorphous form defined by Applicant's claims are not surprising because the salt in the amorphous form Turchetta analyzed appears to have been made by processes significantly different from the processes described in Applicant's Specification. According to the production processes Turchetta describes and claims, Turchetta's sodium risedronate in an amorphous form was prepared by reacting risedronic acid with a base having sodium cations and submitting a solution of the resultant crystalline form of sodium risedronate to lyophilization. See Turchetta's Claim 2 and the supporting Specification [0010-0017].

While Applicant might speculate as to the Examiner's reasons for citing Turchetta and the significance of its teaching to, and the evidentiary weight of, its teaching in support of the rejection under 35 U.S.C. § 103, it is generally improper to do so. As the Examiner is well aware, conclusions as to the patentability or unpatentability of claimed subject matter under 35 U.S.C. § 103 should never be based on speculation. *In re Steele*, 305 F.2d 859, 862 (CCPA 1962).

2. Cazer, Turchetta, Brittain, Threifall, and Muzaffar

Rather, the Examiner's rationale in support of obviousness relies primarily on Cazer's disclosure. The Examiner finds that Cazer "teaches the hydrate forms of the claimed compounds" (OA, p. 3). However, Applicant's Specification (Spec., p. 2, ll. 4-11) and

Turchetta [0003] both distinguish Cazer's crystalline forms of the monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1- bisphosphonic acid, specifically the monohydrate and pentahemihydrate forms thereof, from the monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1- bisphosphonic acid in an amorphous form. According to Applicant (Spec., p. 2, first full para., last two sentences):

Of the two mentioned hydrates, only the pentahemihydrate form is thermodynamically stable. The monohydrate spontaneously transforms to the stable pentahemihydrate.

Unfazed by the distinctions between crystalline and amorphous forms of sodium risedronate identified by Applicant and Turchetta, the Examiner finds that Brittain, Muzaffar, and Threifall generally teach that "compounds can exist in amorphous forms as well as in crystalline forms" (OA, p. 3). Even if we accept the Examiner's finding, it still has not been explained how or why a person having ordinary skill in the art would have concluded that the combined teachings of Cazer, Turchetta, Brittain, Muzaffar, and Threifall support the Examiner's conclusion that Applicant's "claimed amorphous form as well as its . . . properties are suggested by the references" (OA, p. 3). The Examiner's summarily states (OA, p. 3), "It would have been obvious to one skilled in the art in view of the references that the instant compound would exist in different crystalline and noncrystalline forms." The Examiner added that "[n]o unexpected or obvious properties are noted" (OA, p.3). We fail to see how and why the combined teachings would have led a person having ordinary skill in the art to the new amorphous forms Applicant claims.

First, the Examiner points to no specific evidence of record which would have led a person having ordinary skill in the art reasonably to suspect that monosodium risedronate exists in two or more amorphous forms. Turchetta describes one lyophilized amorphous form with the X-ray diffraction pattern shown in Turchetta's Figure 1. Only Applicant describes salts in amorphous and virtually amorphous or semi-crystalline forms which show the X-ray

diffraction patterns defined by Applicant's claims and depicted in Applicant's Figures 4, 9, and 10.

Second, there is evidence in Applicant's Specification (Spec., pp. 11-12, Examples 10 and 11), and Applicant has filed herewith additional evidence in the form of a Declaration Under 37 C.F.R. §1.132 (attached hereto), which show not only that the new amorphous forms of the monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1- bisphosphonic acid Applicant claims exist but also that the new amorphous forms of the monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1- bisphosphonic acid Applicant claims are significantly more stable in hydrochloric acid than Cazer's most stable crystalline hydrate and significantly more soluble in water than Cazer's most stable crystalline hydrate (Cazer's crystalline form is a material from which Applicant's new amorphous forms were produced). Even if we presume that the Examiner correctly found that persons having ordinary skill in the art reasonably would have expected that the monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1- bisphosphonic acid "would exist in different crystalline and noncrystalline forms" (OA, p. 3; emphasis added) without any supporting evidence in the references cited, the prior art reasonably would not have led persons having ordinary skill in the art to suspect that the different noncrystalline forms would be (1) significantly more stable in hydrochloric acid than the pentahemihydrate crystalline form, (2) significantly more soluble in water than the pentahemihydrate crystalline form, and show X-ray diffraction patterns significantly different from the X-ray diffraction pattern of the only other amorphous form of sodium risedronate described in the art the Examiner has cited, i.e., Turchetta's lyophilized amorphous form.

Apparently realizing that the foundation for the obviousness rejection is weak, the Examiner resorts to what appears to be the overruled opinion of the Board in *Ex parte Hartop*, 139 USPQ 525 (Bd. Pat. App. & Int. 1963). The Examiner correctly reports that

Hartop “held that a new crystal form of a known compound was unpatentable because the new crystal form exhibited the same utility as the known forms” (OA, p. 3, second para., last sentence). The Examiner stated (OA, p. 3):

Changing the form, purity or other physical characteristic of an old product does not render the new form patentable where the difference in form, purity or characteristic is inherent or obvious by the prior art. *In re Cofer*, 148 USPQ 268. Mere difference in physical property is a well known conventional variation for the same pure substance (see *Brittain*, p. 1-2) is *prima facie* obvious. Products that are merely a different form of a known compound, having the same utility as the prior art compounds, are unpatentable absent unexpected result.

The problem with the Examiner’s position is that the Court in *In re Cofer*, 354 F.2d 664, 667-668, 148 USPQ 268, 270-271 (CCPA 1968), essentially disavowed *Hartop*’s conclusion.

Discussing the Board’s reliance on *Hartop*’s conclusion, the *Cofer* Court stated, *Id.*

(emphasis added):

We think the record supports [Appellant’s] . . . contentions [“that the record is devoid of any express support for the finding by either the examiner or board that the new physical form . . . would be obvious”]. There is no explanation in the views of the board or examiner why it should be found from the references or from common knowledge that a person skilled in the art would regard free-flowing crystals . . . to be obvious. . . .

. . . The cited cases fail to support . . . [*Hartop*’s] broad proposition that “merely changing the form, purity or another characteristic of an old product, the utility remaining the same as that for the old product, does not render the claimed product patentable.”

The *Cofer* Court stated that common utility is but one factor to be considered in determining obviousness under 35 U.S.C. §103. The Examiner must consider “whether the prior art suggests the particular structure or form of the compound or composition as well as suitable methods of obtaining that structure or form. The new form of the compound set forth in the claims is as much a part of the ‘subject matter as a whole’ to be compared with the prior art as are other properties of the material which make it useful.” *Id.* In short, the Examiner’s position in this case has been overruled.

In this case, there is no evidence which would have led a person having ordinary skill in the art to the subject matter Applicant claims. Applicant has shown that the properties of

Applicant's new forms differ significantly and unexpectedly from the properties of the most stable, most soluble crystalline form known in the art. Applicant has shown that the X-ray diffraction patterns of the claimed new amorphous forms and the methods of synthesizing the claimed new amorphous forms differ significantly from the lyophilized amorphous form taught by Turchetta. In short, the art applied by the Examiner, whether Turchetta is prior art or not, does not reasonably support the Examiner's rejection of Applicant's claims under 35 U.S.C. §103. Accordingly, the rejection should be withdrawn.

Rejections under 35 U.S.C. § 112, 1st paragraph

The Examiner rejected Claims 25-27 under 35 U.S.C. § 112, 1st para., for non-compliance with its written description and enablement requirements (OA, pp. 3-4, bridging para.). Independent Claim 25, as currently amended, is directed to "a pharmaceutical formulation, comprising a monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid in an amorphous form of claim 1 and at least one pharmaceutically acceptable carrier."

The written description requirement of 35 U.S.C. § 112, 1st para., is prima facie satisfied when the specification describes the subject matter claimed in terms which indicate that applicant invented the subject matter claimed. In this case, Applicant's Specification positively states (Spec., p. 4, last full sentence), "[T]he . . . described amorphous forms of risedronate according to this invention are stable at normal conditions and are suitable for preparation of pharmaceutical formulations." The Specification further instructs (Spec., p. 5, ll. 1-14):

[T]he invention includes a pharmaceutical formulation containing amorphous risedronate.

Preferred forms for utilization of amorphous risedronate are oral formulations, especially in the form of tablets. Besides the active substance, suitable diluents, binders, disintegrants and glidants are used to prepare the tablet.

A composition that can be directly compressed is an extraordinarily advantageous combination, where a mixture of mannitol and microcrystalline cellulose plays the role of the diluent. This combination displays exceptional stability, especially in the wet environment.

A dosage form can contain 5 to 35 mg of the active substance, based on pure risedronic acid. Forms of 5 mg for once a day administration and 35 mg for once-a-week administration are the preferable ones.

While the Examiner endeavors to explain why the supporting Specification would not have enabled a person skilled in the art to make and use the full scope of the pharmaceutical compositions of Applicant's Claims 25-27, the Examiner has not explained why Applicant's Specification does not satisfy the written description requirement of 35 U.S.C. §112, 1st para., which is the Office's initial burden.

We repeat, Applicant's Claims 25-27 are directed to "a pharmaceutical formulation comprising a monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid in an amorphous form of claim 1 and at least one pharmaceutically acceptable carrier." Applicant's Specification reasonably describes the same subject matter as Applicant's invention. The Examiner should withdraw the rejection under 35 U.S.C. §112, 1st para., for noncompliance with its written description requirement.

The Examiner's rejection of Claims 25-27 under 35 U.S.C. §112, 1st para., appears to focus on the enablement requirement. The Examiner has the initial burden to provide a reasonable basis to question that Applicant's Specification would not have enabled persons having ordinary skill in the art to make and use the full scope of the subject matter claimed. *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). The Examiner must provide some reason to doubt the objective truth of statements made in the Specification which reasonably appear to enable persons having ordinary skill in the art to make and use the full scope of the subject matter claimed. *In re Marzocchi*, 439 F. 2d 220, 224 (CCPA 1971).

In this case, the Examiner states that "the pharmaceutical formulation field is well aware that amorphous forms when formulated into compositions may undergo

transformation” (OA, p. 4, first full para.). The Examiner cites Doelker for its teaching that amorphous forms of novobiocine acid are thermodynamically unstable and transform into crystalline forms of the same compound (OA, p. 4, first full para.). The Examiner also cites Muzaffar and Theifall for the general view that processes of production affect polymorphism (OA, p. 4, first full para.).

However, the evidence of record does not establish that Applicant’s monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid in an amorphous form would be, or reasonably would have been expected to be, thermodynamically unstable or that the processes of making a monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid in an amorphous form described in Applicant’s Specification would be expected to produce salts which are thermodynamically unstable. To the contrary, Applicant’s Specification teaches that the monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid in an amorphous form claimed is thermodynamically stable in a wet environment and in a dry pharmaceutical carrier and thus suitable for use in the pharmaceutical formulations Applicant claims. See, for example, Applicant’s Examples 2 and 10 and Comparative Test A of the attached Declaration Under 37 CFR §1.132.

The Examiner argues (OA, p. 5), “[H]ydrates may dehydrate. . . . [D]ehydration of hydrates may easily occur” However, Applicant does not claim a crystalline sodium risedronate hydrate.

The Examiner argues (OA, p. 5), “Amorphous forms tend to convert from less stable to more stable forms. No method exists to predict the forms of a solid compound with any significant certainty.” However, Applicant’s Specification teaches, and the evidence of record supports Applicant’s teaching, that the claimed monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid in an amorphous form is stable. Moreover, the Examiner’s finding that the forms of a solid compound cannot be predicted with any

significant certainty tends to support the patentability of Applicant's claims rather than their unpatentability over the applied art.

According to the Examiner, the art cited suggests that the formulation process could cause polymorphic forms to change (OA, p. 5). However, Applicant's Specification teaches, and the examples thereof and declaration evidence show, that Applicant's formulation processes do not destabilize the new amorphous forms claimed.

Next, the Examiner alleges that Applicant may not claim new amorphous forms in terms of their X-ray diffraction patterns, allegedly because compositions including the new amorphous forms change during formulation (OA, p. 6). Applicant's Specification, its examples, and the newly filed declaratory evidence indicate that the stability of the monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid in an amorphous form persists when formulating pharmaceutical compositions therewith. Moreover, Turchetta, the closest art cited by the Examiner, appears to corroborate Applicant's statements regarding the stability of monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid at least with respect to one lyophilized amorphous form and defines that lyophilized amorphous form by its X-ray diffraction pattern.

The Examiner refers to Applicant's claimed monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid in an amorphous forms as "hydrate forms" (OA, p. 6, *The breadth of the claims*). Cazer's monohydrate and pentahemihydrate are hydrate forms. Applicant's new amorphous forms are not hydrate forms. Cazer's crystalline monohydrate is unstable. Moreover, Applicant has shown that the monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid in an amorphous form is not a classic hydrate form, is more soluble than classic hydrate forms, and is more stable than classic hydrate forms in pharmaceutical compositions. The Examiner appears to have erred interpreting the full scope and content of Applicant's claims.

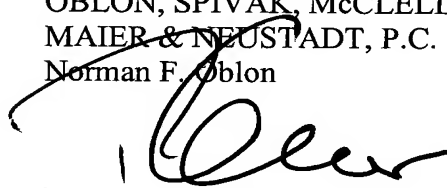
Finally, while the Examiner argues that undue experimentation would have been required for persons having ordinary skill in the art to determine the full scope of pharmaceutical compositions claimed by verifying that the new amorphous forms therein have the X-ray diffraction patterns defined indicated in Applicant's claims, the Examiner's arguments are not supported by any objective evidence. There is no objective evidence relating to unstable forms of monosodium risedronate in any amorphous form in the record. More importantly, there is no objective evidence relating to unstable forms of monosodium risedronat in an amorphous form Applicant's claim. If, as Applicant's Specification teaches, the new amorphous forms claimed are stable enough for pharmaceutical formulation, we do not understand why reverification of the X-ray diffraction patterns of the new amorphous forms in the pharmaceutical formulations claimed would be necessary, and if deemed necessary by a person having ordinary skill in the art, require undue experimentation. Applicant urges the Examiner to withdraw the rejections under 35 U.S.C. §112, 1st para.. There is in this record no evidence that Applicant's disclosure is nonenabling.

Conclusion

For reasons stated herein, Applicant requests that the Examiner withdraw the rejections of Applicant's claims under 35 U.S.C. §112, 2nd para. (Claims 1-9, 14-18, and 25-27), §101/§112 (Claim 15), §112, 1st para. (Claims 25-27), and §103(a)(Claims 1-9 and 25-27) and pass the currently amended claims to issue.

Respectfully submitted,

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